

IN THE CLAIMS:

This listing of claims will replace all prior versions and listing of claims in the application.

Listing of the claims:

Claims 1-12 (**cancelled**).

Claim 13 (**new**): A method for the production of an anti-cancer effect in a warm-blooded mammal in need thereof which comprises the administration of a VEGF receptor tyrosine kinase inhibitor in combination with a Src kinase inhibitor characterised in that:

- (i) an improved anti-cancer effect is obtained; and
- (ii) an appropriate dose of each component of the combination is selected such that the contrasting blood pressure effects associated with the individual use of either component of the combination are substantially counter-balanced;

and wherein the VEGF receptor tyrosine kinase inhibitor is selected from:

4-(4-fluoro-2-methylindol-5-yloxy)-6-methoxy-7-(3-(pyrrolidin-1-yl)propoxy)quinazoline,
4-(4-fluoro-2-methylindol-5-yloxy)-6-methoxy-7-(3-piperidinopropoxy)quinazoline
and
4-(4-bromo-2-fluoroanilino)-6-methoxy-7-(1-methylpiperidin-4-ylmethoxy)quinazoline,

or a pharmaceutically-acceptable acid-addition salt thereof;

and the Src kinase inhibitor is selected from:

4-(6-chloro-2,3-methylenedioxyanilino)-7-[2-(4-methylpiperazin-1-yl)ethoxy]-5-tetrahydropyran-4-yloxyquinazoline,
7-[2-(4-acetylpirazin-1-yl) ethoxy]-4-(6-chloro-2,3-methylenedioxyanilino)-5-isopropoxyquinazoline and
7-[2-(4-acetylpirazin-1-yl)ethoxy]-4-(5-chloro-2,3-methylenedioxypyrid-4-ylamino)-5-isopropoxyquinazoline,
or a pharmaceutically-acceptable acid-addition salt thereof.

Claim 14 (new): A method according to claim 13 wherein the VEGF receptor tyrosine kinase inhibitor is 4-(4-fluoro-2-methylindol-5-yloxy)-6-methoxy-7-(3-(pyrrolidin-1-yl)propoxy)quinazoline, or a pharmaceutically-acceptable acid-addition salt thereof, and the Src kinase inhibitor is 4-(6-chloro-2,3-methylenedioxyanilino)-7-[2-(4-methylpiperazin-1-yl)ethoxy]-5-tetrahydropyran-4-yloxyquinazoline, or a pharmaceutically-acceptable acid-addition salt thereof.

Claim 15 (new): A method according to claim 13 wherein the VEGF receptor tyrosine kinase inhibitor is 4-(4-fluoro-2-methylindol-5-yloxy)-6-methoxy-7-(3-piperidinopropoxy)quinazoline, or a pharmaceutically acceptable acid-addition salt thereof, and the Src kinase inhibitor is 4-(6-chloro-2,3-methylenedioxyanilino)-7-[2-(4-methylpiperazin-1-yl) ethoxy]-5-tetrahydropyran-4-yloxyquinazoline, or a pharmaceutically-acceptable acid-addition salt thereof.

Claim 16 (new): A method according to claim 13 wherein, the VEGF receptor tyrosine kinase inhibitor is 4-(4-bromo-2-fluoroanilino)-6-methoxy-7-(1-methylpiperidin-4-ylmethoxy)quinazoline, or a pharmaceutically-acceptable acid-addition salt thereof, and the Src kinase inhibitor is 4-(6-chloro-2,3-methylenedioxyanilino)-7-[2-(4-methylpiperazin-1-yl)ethoxy]-5-tetrahydropyran-4-yloxyquinazoline, or a pharmaceutically-acceptable acid-addition salt thereof.

Claim 17 (new): A method according to claim 13 wherein the VEGF receptor tyrosine kinase inhibitor is 4-(4-fluoro-2-methylindol-5-yloxy)-6-methoxy-7-(3-(pyrrolidin-1-yl)propoxy)quinazoline, or a pharmaceutically-acceptable acid-addition salt thereof, and the Src kinase inhibitor is 7-[2-(4-acetylpirperazin-1-yl)ethoxy]-4-(6-chloro-2,3-methylenedioxyanilino)-5-isopropoxyquinazoline, or a pharmaceutically-acceptable acid-addition salt thereof.

Claim 18 (new): A method according to claim 13 wherein the VEGF receptor tyrosine kinase inhibitor is 4-(4-fluoro-2-methylindol-5-yloxy)-6-methoxy-7-(3-

piperidinopropoxy)quinazoline, or a pharmaceutically-acceptable acid-addition salt thereof, and the Src kinase inhibitor is 7-[2-(4-acetylpiperazin-1-yl)ethoxy]-4-(6-chloro-2,3-methylenedioxyanilino)-5-isopropoxyquinazoline, or a pharmaceutically-acceptable acid-addition salt thereof.

Claim 19 (new): A method according to claim 13 wherein the VEGF receptor tyrosine kinase inhibitor is 4-(4-bromo-2-fluoroanilino)-6-methoxy-7-(1-methylpiperidin-4-ylmethoxy)quinazoline, or a pharmaceutically-acceptable acid-addition salt thereof, and the Src kinase inhibitor is 7-[2-(4-acetylpiperazin-1-yl)ethoxy]-4-(6-chloro-2,3-methylenedioxyanilino)-5-isopropoxyquinazoline, or a pharmaceutically-acceptable acid-addition salt thereof.

Claim 20 (new): A method according to claim 13 wherein the VEGF receptor tyrosine kinase inhibitor is 4-(4-fluoro-2-methylindol-5-yloxy)-6-methoxy-7-(3-(pyrrolidin-1-yl)propoxy)quinazoline, or a pharmaceutically-acceptable acid-addition salt thereof, and the Src kinase inhibitor is 7-[2-(4-acetylpiperazin-1-yl)ethoxy]-4-(5-chloro-2,3-methylenedioxypyrid-4-ylamino)-5-isopropoxyquinazoline, or a pharmaceutically-acceptable acid-addition salt thereof.

Claim 21 (new): A method according to claim 13 wherein the VEGF receptor tyrosine kinase inhibitor is 4-(4-fluoro-2-methylindol-5-yloxy)-6-methoxy-7-(3-piperidinopropoxy)quinazoline, or a pharmaceutically-acceptable acid-addition salt thereof, and the Src kinase inhibitor is 7-[2-(4-acetylpiperazin-1-yl)ethoxy]-4-(5-chloro-2,3-methylenedioxypyrid-4-ylamino)-5-isopropoxyquinazoline, or a pharmaceutically-acceptable acid-addition salt thereof.

Claim 22 (new): A method according to claim 13 wherein the VEGF receptor tyrosine kinase inhibitor is 4-(4-bromo-2-fluoroanilino)-6-methoxy-7-(1-methylpiperidin-4-ylmethoxy)quinazoline, or a pharmaceutically-acceptable acid-addition salt thereof, and the Src kinase inhibitor is 7-[2-(4-acetylpiperazin-1-yl)ethoxy]-4-(5-chloro-2,3-

methylenedioxypyrid-4-ylamino)-5-isopropoxyquinazoline, or a pharmaceutically-acceptable acid-addition salt thereof.

Claim 23 (**new**): A method for the treatment of a solid tumour disease in a warm-blooded mammal in need thereof which comprises the administration of an effective amount of a VEGF receptor tyrosine kinase inhibitor in combination with an effective amount of a Src kinase inhibitor characterised in that:

- (i) an improved anti-tumour effect is obtained; and
- (ii) an appropriate dose of each component of the combination is selected such that the contrasting blood pressure effects associated with the individual use of either component of the combination are substantially counter-balanced;

and wherein the VEGF receptor tyrosine kinase inhibitor is selected from:

4-(4-fluoro-2-methylindol-5-yloxy)-6-methoxy-7-(3-(pyrrolidin-1-yl)propoxy)quinazoline,
4-(4-fluoro-2-methylindol-5-yloxy)-6-methoxy-7-(3-piperidinopropoxy)quinazoline
and
4-(4-bromo-2-fluoroanilino)-6-methoxy-7-(1-methylpiperidin-4-ylmethoxy)quinazoline,

or a pharmaceutically-acceptable acid-addition salt thereof;

and the Src kinase inhibitor is selected from:

4-(6-chloro-2,3-methylenedioxyanilino)-7-[2-(4-methylpiperazin-1-yl)ethoxy]-5-tetrahydropyran-4-yloxyquinazoline,
7-[2-(4-acetylpirazin-1-yl) ethoxy]-4-(6-chloro-2,3-methylenedioxyanilino)-5-isopropoxyquinazoline and
7-[2-(4-acetylpirazin-1-yl)ethoxy]-4-(5-chloro-2,3-methylenedioxypyrid-4-ylamino)-5-isopropoxyquinazoline,
or a pharmaceutically-acceptable acid-addition salt thereof.

Claim 24 (**new**): The method of claim 13 wherein the cancer is selected from oesophageal cancer, myeloma, hepatocellular, pancreatic and cervical cancer, Ewings

tumour, neuroblastoma, Kaposi's sarcoma, ovarian cancer, breast cancer, colorectal cancer, prostate cancer, bladder cancer, melanoma, non small cell lung cancer (NSCLC), small cell lung cancer (SCLC), gastric cancer, head and neck cancer, brain cancer and renal cancer.

Claim 25 (new): The method of claim 13 or claim 23 wherein the VEGF receptor tyrosine kinase inhibitor and the Src kinase inhibitor are administered for the treatment of a solid tumour cancer.

Claim 26 (new): The method of claim 25 wherein the solid tumour cancer is selected from cancer of the colon, breast, prostate, lungs and skin.

Claim 27 (new): The method of claim 13 or claim 23 wherein the VEGF receptor tyrosine kinase inhibitor and the Src kinase inhibitor are administered simultaneously, sequentially or separately.